REMARKS

Applicant respectfully requests entry of the amendment and reconsideration of the claims. Claim 1 has been amended to further clarify the claimed subject matter. Support for the addition of the term "therapeutic" to claim 1 can be found throughout the specification, including at page 11, line 20 to page 12, line 2. New claim 20 has been added, reflecting the deleted portions of previous claim 1 as a dependent claim. Support for the specific nitric oxide donor compounds can be found throughout the specification, including at page 8, lines 11-15. No new matter has been added through the amendments. Applicant respectfully requests reconsideration and withdrawal of the rejections under 35 U.S.C. § 102(b) and § 112, second paragraph.

Interview Summary

Applicant thanks Examiner Nancy Zhang and Supervisory Patent Examiner Ardin H. Marschel for taking the time to meet on November 16, 2006.

At the meeting, the rejections under 35 U.S.C. § 102(b) and § 112, second paragraph were discussed, and the Supervisory Patent Examiner helpfully suggested an amendment that might overcome the rejections. The breadth of the claims was also discussed, as addressed below.

In an earlier office action mailed April 27, 2005, a previous Examiner rejected claim 1 as being enabled for certain NO donor compounds, but not reasonably enabled for all types of compounds which fall within the scope of "nitric oxide donors". In support of this rejection, the previous rejection quoted *In re Dreshfield*, giving the general rule

> It is well settled in cases involving chemicals and chemical compounds, which differ radically in their properties, it must appear in an applicant's specification either by the enumeration of a sufficient number of the members of a group or by other appropriate language, that the chemicals or chemical compounds included in the claims are capable of accomplishing the desired result." Moreover, the court has held "cases involving unpredictable factors, such as chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the *degree of unpredictability* of the factors involved.

In response to this rejection, Applicant eventually amended claim 1 to claim specific nitric oxide donor compounds listed in the application.

However, after discussions with the inventor, and after considering published reviews of NO donor compounds, Applicant has found that

> [a]ll nitrovasodilators act intracellularly by a common molecular mechanism. This is characterized by the release of nitric oxide (NO). They are, thus, prodrugs or carriers of the active principle NO, responsible for endothelial controlled vasodilation...Chemically, they represent a very heterogeneous group of substances which, nevertheless, all seem to exert their pharmacodynamic action by an identical final step of bioactivation, i.e. the release of nitric oxide (NO). [emphasis added] (Noack & Feelisch, "Molecular mechanisms of nitrovasodilator bioactivation", *Basic Research Cardiology* (1991) 86:37-50; copy attached).

Similarly, from another review paper, "[b]y definition, all NO donors produce NO-related activity when applied to biological systems and are thus principally suited to either mimic an endogenous NO-related response or substitute for an endogenous NO deficiency" (Feelisch, "The use of nitric oxide donors in pharmacological studies", *Naunyn-Schmiedeberg's Arch Pharmacol* (1998) 358:113-122; copy attached).

In other words, nitric oxide donors are compounds that are well known that produce nitric oxide *in vivo*. These compounds could be referred to as nitric oxide donors, nitric oxide prodrugs, nitric oxide generators, or nitric oxide equivalents. The essential point is nitric oxide donors do not need be addressed specifically by compound name in the independent claim since nitric oxide donors are so well known and their mechanism of action is consistent. The "degree of unpredictably" is, in essence, zero. In all cases, these compounds act by entering the body, wherein the nitric oxide group is released, and the nitric oxide acts *in vivo*. Thus, these are properly characterized as prodrugs for nitric oxide, and all therapeutic nitric oxide donors are encompassed within the scope of the present invention. Favourable consideration of the currently amended claim 1 is respectfully requested.

Rejection under 35 U.S.C. § 112, second paragraph

The Examiner rejects claims 1-3 and 19 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. The Examiner stated that the phrase "administering to a patient an effective amount" is indefinite. The Examiner further contends that having the phrase "increasing

insulin sensitivity in a mammalian patient in need thereof" in the preamble and not the body of claim 1 implies what is meant for "effective". In response, and as suggested by the Examiner in the interview, Applicant has amended the phrase "a patient" to read "the patient". By this change in antecedent basis, "the patient" references the phrase in the preamble of claim 1, specifically "increasing insulin sensitivity in a mammalian patient in need thereof". As discussed with the Examiner in the interview, this amendment should overcome the rejection. Applicant respectfully requests removal of this rejection.

Rejection under 35 U.S.C. § 102(b)

The Examiner rejects claims 1-3 and 19 under 35 U.S.C. § 102(b) as allegedly anticipated by U.S. Patent No. 5,234,956 (Lipton). The Examiner states that Lipton teaches a method for reducing NMDA receptor-mediated neuronal damage in a mammal by administering to the mammal a nitric-oxide generating compound such as nitroprusside. The Examiner asserts that the phrase "increasing insulin sensitivity in a mammalian patient in need thereof" is merely in the preamble, and thereby further asserts that the instantly claimed method is anticipated.
As discussed above and with the Examiner in the interview, the current amendment of "to <u>the</u> patient" now references a patient in need of increased insulin sensitivity. Applicant respectfully asserts that amended claim 1 and dependent claims 2-3 and 19 are not anticipated by the '956 patent. In view of the foregoing, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(b).

Summary

In view of the above amendments and remarks, the applicant respectfully requests a Notice of Allowance. If the Examiner believes a telephone conference would advance prosecution of this application, the Examiner is invited to telephone the undersigned at the below listed telephone number.

Respectfully submitted,

MERCHANT & GOULD P.C.
P.O. Box 2903
Minneapolis, Minnesota 55402-0903
(612) 332-5300

Date: February 21, 2007

Brian R. Dorn
Reg. No. 57,395